Magnetic Resonance Imaging Tracking of Ferumoxytol-Labeled Human Neural Stem Cells: Studies Leading to Clinical Use.

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Public Summary:
Numerous stem cell-based therapies are currently under clinical investigation, including the use of neural stem cells (NSCs) as delivery vehicles to target therapeutic agents to invasive brain tumors. The ability to monitor the time course, migration, and distribution of stem cells following transplantation into patients would provide critical information for optimizing treatment regimens. No effective cell-tracking methodology has yet garnered clinical acceptance. A highly promising noninvasive method for monitoring NSCs and potentially other cell types in vivo involves preloading them with ultrasmall superparamagnetic iron oxide nanoparticles (USPIOs) to enable cell tracking using magnetic resonance imaging (MRI). We report here the preclinical studies that led to U.S. Food and Drug Administration approval for first-in-human investigational use of ferumoxytol to label NSCs prior to transplantation into brain tumor patients, followed by surveillance serial MRI. A combination of heparin, protamine sulfate, and ferumoxytol (HPF) was used to label the NSCs. HPF labeling did not affect cell viability, growth kinetics, or tumor tropism in vitro, and it enabled MRI visualization of NSC distribution within orthotopic glioma xenografts. MRI revealed dynamic in vivo NSC distribution at multiple time points following intracerebral or intravenous injection into glioma-bearing mice that correlated with histological analysis. Preclinical safety/toxicity studies of intracerebrally administered HPF-labeled NSCs in mice were also performed, and they showed no significant clinical or behavioral changes, no neuronal or systemic toxicities, and no abnormal accumulation of iron in the liver or spleen. These studies support the clinical use of ferumoxytol labeling of cells for post-transplant MRI visualization and tracking.

Scientific Abstract:
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